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DNA/BSA binding study of mononuclear gold(III) complex with azaconazole

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INTRODUCTION & AIM

Nitrogen-containing aromatic heterocycles have garnered significant interest as essential scaffolds in the synthesis of bioactive compounds, owing to their broad applications in various pharmacological fields, including vitamins, herbicides, antifungal, antibacterial, and anticancer agents. Their unique structural and electronic properties allow them to interact effectively with biological targets, making them attractive ligands in the design of metal-based therapeutic agents. In the present study, azaconazole (acz) was employed for the synthesis of a mononuclear gold(III) complex, [$AuCl_3$(acz)] (Figure 1). The complex suitable for X-ray diffraction analysis (Figure 2) was obtained by reacting equimolar amounts of potassium tetrachloridoaurate(III) and the acz ligand under reflux conditions for 3 h. In this complex, azaconazole coordinates monodentately to the Au(III) ion, while the remaining coordination sites in the square-planar geometry are occupied by chloride ions. The interaction between the synthesized gold(III) complex and calf thymus DNA (ct-DNA) was investigated using fluorescence emission spectroscopy in the presence of the intercalative agent ethidium bromide (EthBr) and the minor groove binder Hoechst 33258 (Hoe) Figure 3 and Table 1. Additionally, fluorescence competition experiments were performed using specific site markers, including eosin Y, ibuprofen, and digitoxin, to gain deeper insight into the binding sites on BSA (Figure 4 and Table 2). Eosin Y is known as a marker for site I (subdomain IIA), ibuprofen for site II (subdomain IIIA), and digitoxin for site III (subdomain IB).

METHOD

- Stock solutions of complex was prepared in DMF (1.0×10^{-2} M)
- The interaction of the compound with bovine serum albumin (BSA) and calf thymus DNA (ct-DNA) was investigated using fluorescence emission spectroscopy on a Shimadzu RF-6000 spectrofluorometer

- The BSA binding study was conducted using tryptophan fluorescence quenching experiments in phosphate-buffered saline (PBS, pH 7.4) at room temperature. Fluorescence emission spectra were recorded in the range of 295–500 nm with an excitation wavelength of 290 nm. The concentration of BSA was maintained at 3.6 μM, while the concentration of the complex was gradually increased from 0 to 19.7 μM

- Competitive binding experiments were performed using specific site markers. Each marker was mixed with BSA in equimolar amounts, followed by titration with increasing concentrations of the complex. The excitation and emission settings were maintained as described previously

- DNA binding experiments were also carried out in PBS, maintaining [ct-DNA]/[Hoe] = 10 and [ct-DNA]/[EthBr] = 10 while increasing the concentrations of the gold(III) complex. Measurements in the presence of Hoe were performed in the wavelength range of 351–750 nm, with an excitation wavelength of 346 nm, whereas measurements in the presence of EthBr were carried out in the wavelength range of 525–750 nm, with an excitation wavelength of 520 nm

RESULTS & DISCUSSION

DNA Binding Study

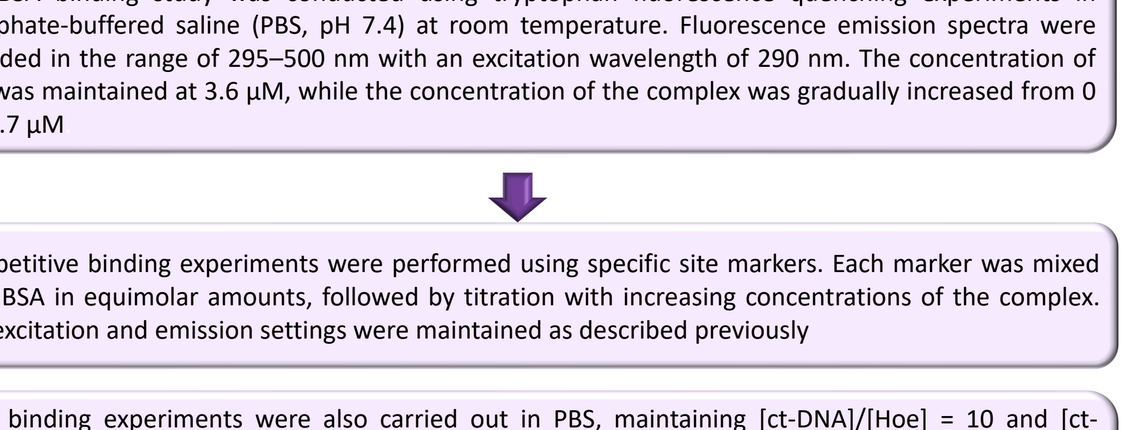

Figure 3. Fluorescence emission spectra of the ct-DNA–Hoe system in the presence of increasing concentrations of the gold(III) complex. The red arrow indicates the changes in intensity following the addition of the complex. Inset: Stern–Volmer plot of F_0/F versus [complex]

Table 1. The value of the binding constants of complex with Hoe-ct-DNA system

	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	n
complex– ct DNA - Hoe	**(4.32 ± 0.0) × 10^4**	**52,04**	**4.32 × 10^{12}**	**2.80 × 10^5**	**1.91**

ACKNOWLEDGEMENTS

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RESULTS & DISCUSSION

Synthesis

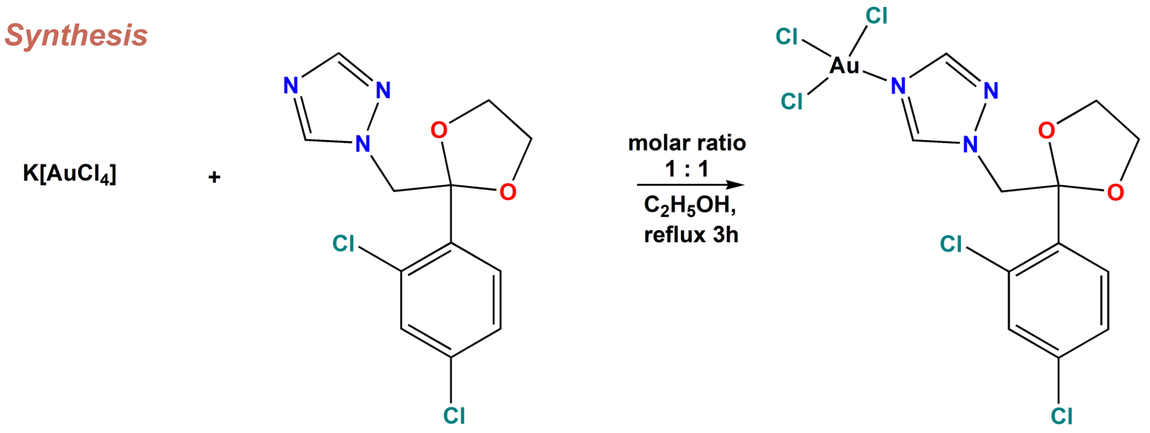

Figure 1. Schematic presentation of the reaction for the synthesis of gold(III) complex

BSA Binding Study and Competitive Experiments with BSA Site Markers

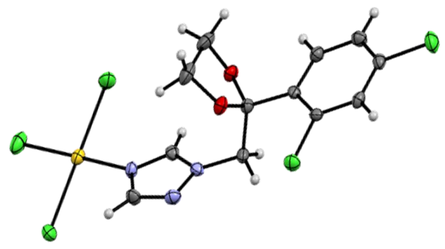

Figure. 2. Crystal structure of gold(III) complex

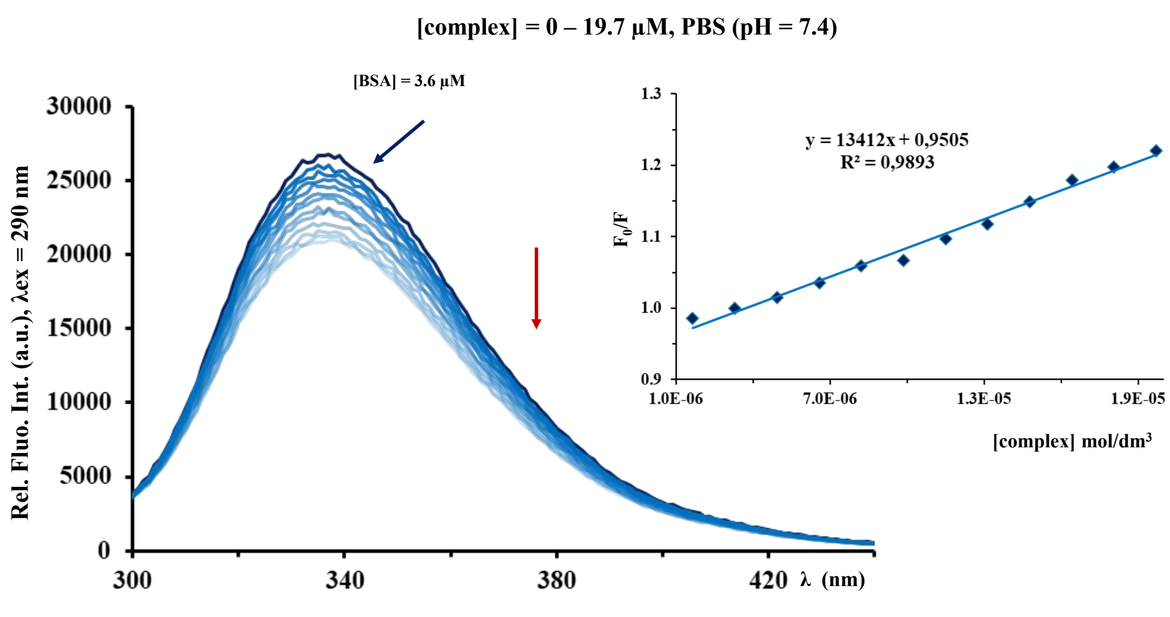

Figure 4. Fluorescence emission spectra of BSA in the presence of an increasing concentration of gold(III) complex. The red arrow shows the changes of the intensity after the addition of the complex. Inserted graph: Stern-Volmer plot of F_0/F *vs*. [complex].

Table 2. Values of the BSA binding data for gold(III) complex in the absence and presence of the site markers, eosin Y (eos Y), ibuprofen (ibu) and digitoxin (dig)

	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	*n*
complex– BSA	**(1.40 ± 0.005) × 10^4**	**21.82**	**1.40 × 10^{12}**	**4.70 × 10^3**	**0.91**
complex – BSA – eos Y	**(6.12 ± 0.008) × 10^3**	**12.20**	**6.12 × 10^{11}**	**9.90 × 10^2**	**0.81**
complex – BSA – ibu	**(2.41 ± 0.007) × 10^4**	**33.49**	**2.41 × 10^{12}**	**7.03 × 10^3**	**0.88**
complex – BSA – dig	**(2.02 ± 0.008) × 10^4**	**32.09**	**2.02 × 10^{12}**	**4.15 × 10^4**	**0.84**

CONCLUSION

- The value of the binding constant K_A for the gold(III) complex indicates its binding to BSA, suggesting that this complex can be transported to the target cells
- The investigated gold(III) complex in the presence of eosin Y bind to site I of subdomain IIA with moderately strong affinity.
- The gold(III) complex exhibits high binding affinity toward the minor groove of ct-DNA. However, after the addition of the complex, no significant decrease in the intensity of the DNA - ethidium bromide system was observed, indicating that the complex does not behave as an intercalator.

FUTURE WORK

- Further work will focus on molecular docking studies, as well as on the antimicrobial and cytotoxic evaluation of the gold(III) complex